CLAIMS

1. A method of encapsulating an active substance in a biodegradable polymer, which comprises:

a) dissolving said biodegradable polymer in an organic solvent therefor;

b_1) dispersing said active substance in the organic solution obtained in step a), to provide a dispersion with the active substance as the inner phase thereof; or alternatively

b_2) emulsifying said active substance, dissolved in water or other aqueous solvent therefor, in the organic solution obtained in step a), to provide an emulsion with the active substance as the inner aqueous phase thereof; and

c) subjecting the dispersion obtained in step b_1), or alternatively the emulsion obtained in step b_2), to an encapsulation operation with an aqueous polyethylene glycol solution as a continuous phase, such that micro- or nanoparticles having the active substance encapsulated therein are obtained.

2. A method according to claim 1, wherein the microencapsulation operation in step c) is performed in the presence of an aqueous polyethylene glycol solution having a polyethylene glycol concentration within the range of 20-80% (w/w), preferably 20-60% (w/w), such as 30-55% (w/w) or 30-50% (w/w).

3. A method according to ~~any one of claims 1 and 2~~ Claim 1, wherein the polyethylene glycol has a molecular weight of about 1000 to 40000 Da, preferably about 5000 to 35000 Da.

4. A method according to ~~any one of claims 1, 2 and 3,~~ Claim 1 wherein the encapsulation operation in step c) is performed by adding the dispersion obtained in step b_1), or alternatively the emulsion obtained in step b_2), to said aqueous polyethylene glycol solution while subjecting last-mentioned aqueous solution to a stirring and/or ho-

mogenization operation.

5. A method according to claim 4, wherein the stirring and/or homogenization operation is performed by a low intensity and/or low energy process, e.g. propeller mixing or the use of motionless mixers.

6. A method according to ~~any one of the preceding claims~~ claim 1, wherein said encapsulation operation in step c) is performed in the absence of any surfactant.

7. A method according to ~~any one of the preceding claims~~ claim 1, wherein said biodegradable polymer is insoluble, or slightly soluble, in the aqueous polyethylene glycol solution used in step c), preferably an aliphatic polyester.

8. ~~A method according to any one of the preceding claims~~ claim 1, wherein said biodegradable polymer has a weight average molecular weight in the range of about 2000 to 200 000, preferably about 2000 to 110 000.

9. A method according to any one of the preceding claims, wherein said biodegradable polymer is selected from homo or copolymers prepared from α-hydroxy acids, preferably lactic acid and glycolic acid, and/or cyclic dimers of α-hydroxy acids, preferably lactides and glycolides.

10. A method according to claim 9, wherein a copolymer of lactic acid/glycolic acid or a mixture of polylactic acid/polyglycolic acid is used as said biodegradable polymer, the weight ratio of (poly)lactic acid/(poly)glycolic acid being within the range of about 99/1 to 35/65, preferably 95/5 to 50/50.

11. A method according to ~~any one of the preceding claims~~ claim 1, wherein said organic solvent used in step a) is immiscible or essentially immiscible with said aqueous polyethylene glycol solution used in step c), but slightly or very slightly soluble therein, and capable of dissolving said biodegradable polymer, and is preferably selected from ethyl acetate, dichloromethane, methyl ethyl ketone and/or methyl isobutyl ketone.

12. A method according to ~~any one of the preceding claims~~ Claim 1, wherein the active substance which is dispersed in step b_1) has a particle size within the range of about 0.5-20 µm, preferably 0.5-10 µm, more preferably 0.5-3 µm.

13. A method according to ~~any one of the preceding claims~~ Claim 1, wherein said active substance is a biologically active substance, which is preferably selected from proteins, (poly)peptides, (poly)nucleotides, plasmides and DNA.

14. A method according to claim 13, wherein said biologically active substance is selected from growth hormone, erythropoictin, interferon (α,β,γ-type), vaccine, epidermal growth hormone, Factor VIII, LHRH analoque, insulin, macrophage colony stimulating factor, granulocyte colony stimulating factor and interleukin.

15. A method according to ~~any one of claims 1-12~~ Claim 1, wherein said active substance is a biologically active substance in the form of a non-protein drug selected from the following groups:
anti-tumor agents, antibiotics, anti-flammatory agents, antihistamines, sedatives, muscle relaxants, antiepileptic agents, antidepressants, antiallergic agents, bronchodilators, cardiotonics, antiarrythmic agents, vasodilators, antidiabetic agents, anticoagulants, hemostatics, narcotic agents and steroids.

16. A method according to ~~any one of claims 1-12~~ Claim 1, wherein said active substance is a non-biological substance, which is preferably selected from pesticide, fragrance, flavouring agent, catalyst and herbicide.

17. A method according to ~~any one of the preceding claims~~ Claim 1, wherein the amount of said active substance is in the range of about 0.001% to 90%, preferably about 0.01% to 70%, more preferably about 0.1 to 45%, and most preferably about 0.1 to 40%, said percentage being by weight based on the weight of the final particles.

18. A method according to any one of the preceding

claims, wherein the particles obtained in step c) are separated from said continuous phase, preferably by centrifugation or filtration followed by rinsing with water or other aqueous medium, and dried or allowed to dry, for instance in a vacuum, in the presence of a nitrogen gas flow, by lyophilisation or by air suspension drying.

19. A method according to any ~~one of the preceding claims~~ claim 1, wherein step c) is performed such that the particles obtained are microspheres or capsules or nanospheres or capsules.

20. A method according to claim 19, wherein said particles have a mean diameter in the range of 10-200 µm, preferably 20-100 µm.

21. Sustained release micro or nanoparticles containing an active substance encapsulated in a biodegradable polymer, ~~obtainable by a method according to any one of claims 1-20.~~ obtained by the method of claim 1

22. Particles according to claim 21, which are suitable for parenteral, nasal, pulmonal or oral administration of said active substance.

add B6

add E1